

REMARKS

In the Office Action the Examiner rejected Claims 1-4, 6-9, and 14-16 under 35 U.S.C. §103(a) as being unpatentable over **Lin et al.** (U.S. Patent No. 5,459,030) and **Shanbrom** (U.S. Patent No. 5,985,260) or **Shanbrom** (WO 9822151) or **Piechocki et al.** (U.S. Patent No. 5,660,731) for obviousness. The Examiner objected to Claims 5 and 10 as being based on rejected base claims. The Examiner found that these claims would be allowable because the prior art did not teach a method involving the removal of sodium citrate.

In his rejection the Examiner stated that **Lin et al.** taught a method of inactivating bacteria in platelet or blood preparations comprising applying sodium citrate to the preparation. The Examiner found that this reference did not teach a method comprising iodine or methylene blue. These items, however, are taught in the **Piechocki et al.** and/or **Piechocki et al.** references. The Examiner recognized that Claims 4 and 9 call for concentrations of sodium citrate much higher than that taught in **Lin et al.** because the Examiner contended that “[w]ith respect to the amount of ingredients used, an artisan would have accomplished this optimization through routine experimentation.” Applicant respectfully traverses this contention and the entire obviousness rejection.

The specification teaches that it is well-known to use approximately 0.4% by weight of sodium citrate as an anticoagulant. This amount of citrate has been used for a number of years. There is no indication in any of the prior art that there is any advantage to increasing this amount of citrate. Certainly, there is no indication that an

increased level of citrate results in enhancement to known disinfecting agents. The present specification teaches that enhanced disinfection occurs with amounts of citrate exceeding 1% by weight and preferably 2 % or more by weight. Applicant was unable to find a falling off of the citrate effect at very high concentrations, but the claims have been capped at 15% citrate because concentrations above that are not biologically feasible.

**Lin et al.** teach a method of photoinactivation of bacteria employing psoralens. There is no teaching that the inclusion of 0.4% sodium citrate in the medium enhances the effect of the photoinactivation. In light of the teaching of the present specification it is very unlikely that any enhancement occurs since the present invention teaches that concentration of sodium citrate of **at least 1%** by weight are required to see any effect. A major objective of **Lin et al.** was to reduce the amount of light energy and psoralen needed to inactivate bacteria. Therefore, it is most likely that had there been any enhancing effect of 0.4% sodium citrate, **Lin et al.** would have recognized it. At the same time if routine "optimization" would lead to use of a high level of citrate, **Lin et al** might have been expected to discover the advantages of a higher level of citrate.

Neither of the two **Shanbrom** references specifically refer to use of citrate. Further, the PCT reference is primarily directed to the removal of iodine after disinfecting a solution. Because citrate is often used as an anticoagulant (at about 0.4%) it is possible that some of the experiments described in those references might have contained that level of citrate. However, that is below the level of citrate required

to observe any enhancement of the disinfecting effect. Similarly, **Piechocki et al.** teaches a method for removing dye (methylene blue) usually after photoactivation of the dye. There is no mention of citrate although again it is possible that some of the solutions treated contain citrate as an anticoagulant. Certainly, there was no recognition by **Piechocki et al.** that citrate had any effect whatsoever on the disinfecting process.

The present applicant has made the unexpected discovery that increased concentrations of citrate result in rather significant enhancement of a number of different disinfecting systems. This effect applies to both bacterial and virus. There is no indication of this effect in any of the cited prior art. The Examiner attempts to finesse this by stating that an ordinary worker would arrive at the higher citrate concentration in optimizing the formulae. This is not a proper obviousness rejection. Apart from the present specification there is no teaching that increasing citrate (to at least twice the normally used concentration) would result in enhanced disinfecting. Certainly, all the workers cited by the Examiner had a strong motivation to improve the disinfecting of their processes. However, they all failed to suggest that a significant increase in citrate would achieve this end. Similarly, an ordinary worker would not be expected to double the concentration of a component not known to have any effect on disinfecting in an attempt to optimize a disinfecting formula.

Although **Lin et al.** did not teach that citrate enhances their disinfecting process, Claim 1, as originally drafted, inadvertently overlapped the normally used citrate concentration (the 1-15% limitation was omitted). This has been now corrected in the

amended claims. All of the claims call for an enhancement brought about by citrate concentrations at least twice as high as those used for anticoagulation. As explained above, no references teach any enhancement caused by increases in the citrate concentration. Therefore, Applicant respectfully requests the Examiner to withdraw the claim rejections under 35 U.S.C. §103(a). In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Reexamination and reconsideration of the application, as amended, are requested.

If for any reason the Examiner still finds the application other than in condition for allowance, the Examiner is requested to call the undersigned attorney at the Los Angeles telephone number (310) 734-5403 to discuss the steps necessary for placing the application in condition for allowance. You are hereby authorized to charge any fees due and refund any surplus fees to our Deposit Account No. 50-1796, referencing docket number 25864.05500.

Respectfully submitted,

CROSBY, HEAFEY, ROACH & MAY

Date: 18 October 2001

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Red-lined Claim Copy (Revised Rule 121)

1. (Amended) A method for enhancing the effectiveness of antimicrobial agents comprising the step of combining the antimicrobial agent with at least 1% by weight citric acid and or salts or citric acid.